PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 0256wo210	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/DK 03/00127	International filing date *(day/month/year)* 28.02.2003	Priority date *(day/month/year)* 12.03.2002
International Patent Classification (IPC) or both national classification and IPC A61K38/21		
Applicant MAXYGEN APS et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
02.10.2003	17.06.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Böhmerova, E Telephone No. +49 89 2399-7859

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/DK 03/00127

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-60 as originally filed

Claims, Numbers

1-46 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 39-44

because:

☒ the said international application, or the said claims Nos. 39-44 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1,6,39,44
	No:	Claims	-
Inventive step (IS)	Yes:	Claims	-
	No:	Claims	1,6,39,44
Industrial applicability (IA)	Yes:	Claims	1,6
	No:	Claims	-

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Independent claims 39, 44 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Cited documents

Reference is made to the following documents:

D1: EP-A-0 797 998 (TORAY INDUSTRIES) 1 October 1997

D2: PATENT ABSTRACTS OF JAPAN vol. 1997, no. 10, 31 October 1997 (1997-10-31) & JP 09 151137 A (TORAY IND INC), 10 June 1997

D3: WOUTER B VELDHUIS: 'Delayed treatment with interferon-beta protects against ischemic stroke' STROKE, vol. 33, January 2002, page 346 XP002265895

Unless indicated otherwise reference is made to the passages considered relevant in the search report.

Novelty

Subject-matter of independent claims 1, 6, 39, 44 is considered to be novel under Art. 33(1) and (2) PCT for the following reasons:

Present claims are directed to the use of an interferon beta (IFNB) polypeptide variant comprising an amino acid sequence which differs from the amino acid sequence of wild-type human IFNB in that at least one glycosylation site has been introduced.

D1 discloses an agent for protecting endothelial cells comprising IFNB as an effective ingredient. The agent is used for the treatment of cardiovascular diseases including

brain infarction. D1 teaches exclusively the use of a natural IFNB, no IFNB with an introduced glycosylation site is disclosed.

D2 discloses the use of natural IFNB for inhibition of smooth muscle cell proliferation, no IFNB with an introduced glycosylation site is disclosed. The list of diseases caused by abnormal vascular smooth muscle cells as present in D2 does not comprise stroke, cerebrovascular accident or transient ischemic attack.

D3 discloses the treatment of ischemic stroke with IFNB. However, D3 fails to disclose the use of IFNB with introduced glycosylation site.

Inventiveness

The subject-matter of independent claim 1, 6, 39, 44 is considered as lacking an inventive step under Art. 33(1) and (3) PCT for the following reasons:

The problem to be solved by the present application can be defined as to provide a remedy for the treatment of stroke, cerebrovascular accident (CVA) or transient ischemic attack in a primate.

The solution proposed by the present claims is the use of an interferon beta (IFNB) polypeptide variant comprising an amino acid sequence which differs from the amino acid sequence of wild-type human IFNB in that at least one glycosylation site has been introduced.

However, the claimed solution has not been shown to solve the above defined technical problem. The application comprises no experimental data proving the claimed effect of IFNB variant with an introduced glycosylation site in the treatment of stroke, CVA and/or transient ischemic attack. As the technical problem has not been solved, no inventiveness can be acknowledged.

The solution known from the prior art is the use of natural IFNB (see D1 and D3). The solution proposed by the present claims differs over that known form D1 and D3 in that an IFNB variant comprising at least one introduced glycosylation site is used rather that the natural IFNB. However, the introduction of the glycosylation site to the sequence of natural IFNB is not shown to provide for any technical effect. Consequently, the solution proposed by the present claims represents a simple modification of the solution known

from the prior art without any technical effect which cannot be considered as involving an inventive step.

Industrial applicability

Subject-matter of independent claims 1, 6 is considered to be industrially applicable under Art. 33(1) and (4) PCT.

For the assessment of the present claims 39, 44 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.